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NEWS 4	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 5	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 6	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 7	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 8	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS 9	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS 10	SEP 22	DIPPR file reloaded
NEWS 11	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS 12	SEP 29	DISSABS now available on STN
NEWS 13	OCT 10	PCTFULL: Two new display fields added
NEWS 14	OCT 21	BIOSIS file reloaded and enhanced
NEWS 15	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 16	NOV 24	MSDS-CCOHS file reloaded

NEWS EXPRESS	NOVEMBER 14 CURRENT WINDOWS VERSION IS V6.01c, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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NEWS INTER	General Internet Information
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FILE 'HOME' ENTERED AT 14:09:52 ON 29 NOV 2003

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:10:02 ON 29 NOV 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 NOV 2003 HIGHEST RN 622010-69-9
DICTIONARY FILE UPDATES: 28 NOV 2003 HIGHEST RN 622010-69-9

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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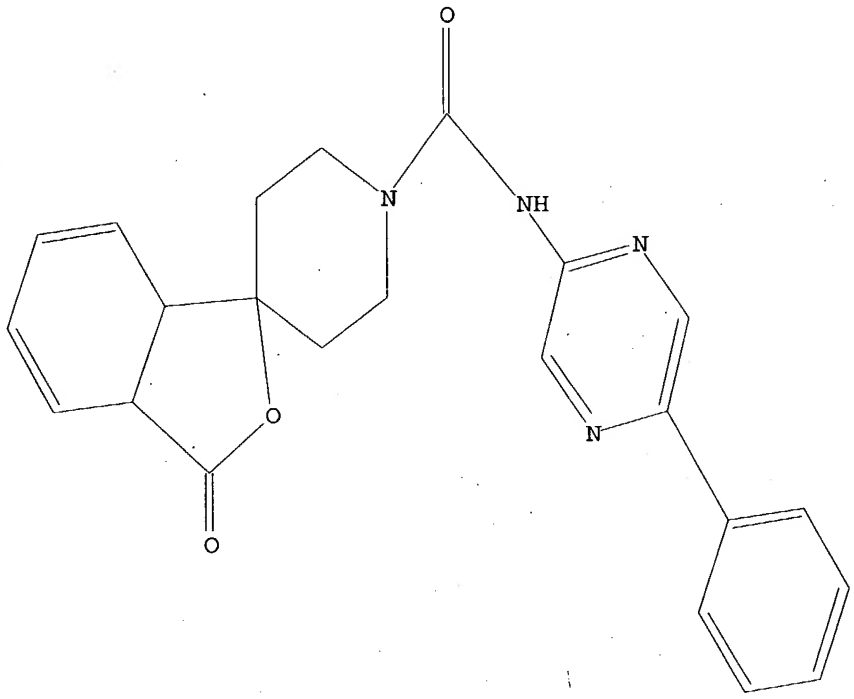
Uploading 10054413.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 14:10:37 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:             1 TO        80
PROJECTED ANSWERS:                0 TO         0

L2             0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 14:10:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      21 TO ITERATE

100.0% PROCESSED      21 ITERATIONS                                 8 ANSWERS
SEARCH TIME: 00.00.01

L3             8 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     148.15     148.36

FILE 'CAPLUS' ENTERED AT 14:10:48 ON 29 NOV 2003
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FILE COVERS 1907 - 29 Nov 2003  VOL 139 ISS 23
FILE LAST UPDATED: 28 Nov 2003  (20031128/ED)

  This file contains CAS Registry Numbers for easy and accurate
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=> s l3
L4             3 L3

=> s l4/prep
FIELD CODES CANNOT BE CHANGED HERE
You may have tried to apply a field code to a term that already has a
field code.  You can only add a field code to a term that has no field
code appended to it.

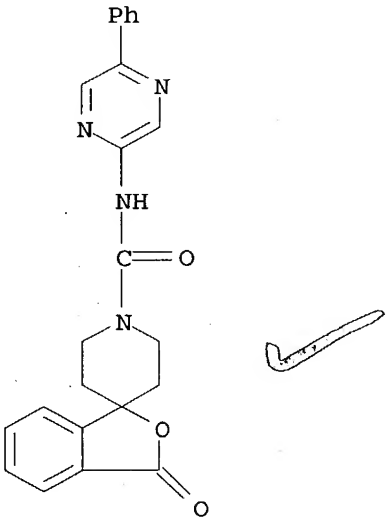
=> d l4 hitstr, iall 1-3

L4   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2003 ACS on STN
IT   328233-00-7P
     RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of spiroisoindolinepiperidinecarboxamides,
        spirocyclohexaneisobenzofurancarboxamides,
        spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as
```

neuropeptide Y antagonists)

RN 328233-00-7 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



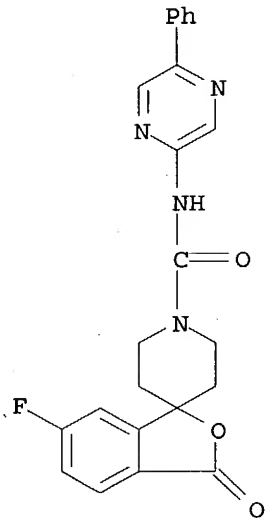
IT **328232-34-4P 328232-36-6P 328232-57-1P 328232-58-2P 328232-61-7P 328232-62-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

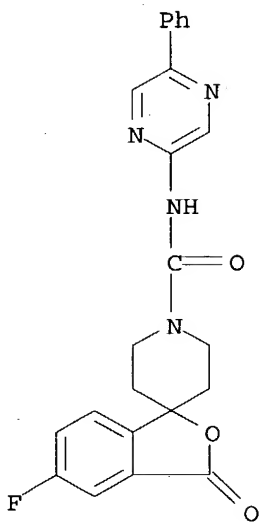
RN 328232-34-4 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 6-fluoro-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 328232-36-6 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 5-fluoro-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



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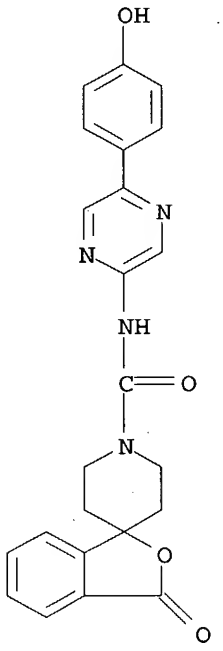

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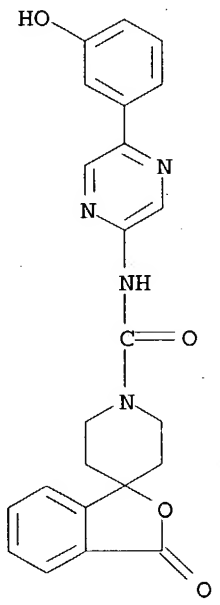
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, N-[5-(3-hydroxyphenyl)pyrazinyl]-3-oxo- (9CI) (CA INDEX NAME)



RN 328232-61-7 CAPLUS
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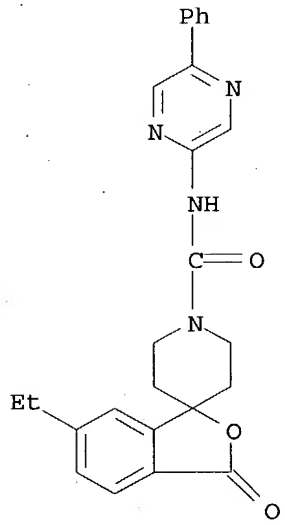
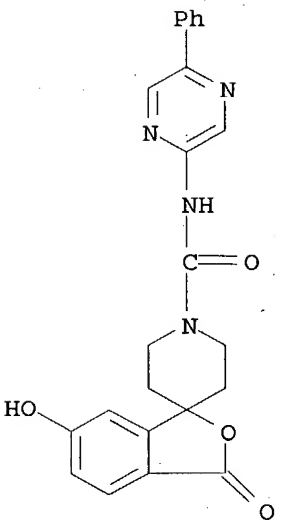


RN 328232-62-8 CAPLUS
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 6-hydroxy-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2002:947029 CAPLUS
DOCUMENT NUMBER: 138:24705
TITLE: Preparation of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compounds as neuropeptide Y antagonists
INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro
PATENT ASSIGNEE(S): Japan
SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Pat. Appl. 2002 52,371.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D487-20
SECONDARY: C07D471-20
US PATENT CLASSIF.: 544230000; 546017000; 546018000
CLASSIFICATION: 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002188124	A1	20021212	US 2002-92549	20020308
JP 2003104884	A2	20030409	JP 2002-271261	20000817
US 6326375	B1	20011204	US 2000-640784	20000818
US 6335345	B1	20020101	US 2001-928431	20010814
US 2002052371	A1	20020502	US 2001-983598	20011025
US 6388077	B2	20020514		
US 6462053	B1	20021008	US 2002-101221	20020320
US 2002165391	A1	20021107		
US 2003055251	A1	20030320	US 2002-226225	20020823
US 6649624	B2	20031118		
WO 2003076443	A1	20030918	WO 2003-JP2611	20030305

W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GH, HR, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SC, SG, TJ, TM, TN, TT, UA, US, UZ, VC, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003220499 A1 20031127 US 2003-453737 20030604

PRIORITY APPLN. INFO.:

JP 1999-233573	A	19990820
JP 2000-137692	A	20000510
US 2000-640784	A3	20000818
US 2001-983598	A2	20011025
JP 2000-247145	A3	20000817
US 2002-92549	A	20020308
US 2002-101221	A3	20020320
US 2002-226225	A3	20020823

OTHER SOURCE(S): MARPAT 138:24705

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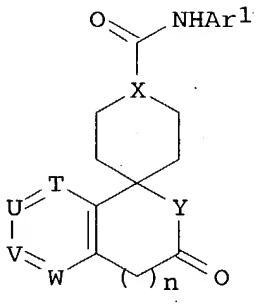

I

ABSTRACT:

Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = CH, CH(OH); Y = (substituted) imino, O], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide (II), which inhibited [125I]neuropeptide Y binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

SUPPL. TERM: spiroisoindolinepiperidinecarboxamide prepn npy antagonist; spirocyclohexaneisobenzofurancarboxamide spiroazaisobenzofurancyclohexanecarboxamide prepn neuropeptide Y receptor antagonist; antidiabetic spirocyclohexaneisobenzofurancarboxamide spiroazaisobenzofurancyclohexanecarboxamide prepn; antiobesity agent spirocyclohexaneisobenzofurancarboxamide spiroazaisobenzofurancyclohexanecarboxamide prepn; bulimia treatment spirocyclohexaneisobenzofurancarboxamide spiroazaisobenzofurancyclohexanecarboxamide prepn

INDEX TERM: Appetite
(bulimia, treatment; prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: Antidiabetic agents

Antiobesity agents
Human
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: Diabetes mellitus
Obesity
(treatment; prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 82785-45-3, Neuropeptide y
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 328232-26-4P 328232-65-1P **328233-00-7P**
ROLE: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

328231-96-5P	328231-97-6P	328231-98-7P	328231-99-8P
328232-00-4P	328232-01-5P	328232-02-6P	328232-03-7P
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478014-12-9P 478014-13-0P 478014-14-1P 478014-15-2P
478014-16-3P 478014-17-4P 478014-18-5P 478014-19-6P
478014-20-9P 478014-21-0P 478014-22-1P 478014-23-2P
478014-24-3P 478014-25-4P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 478014-26-5P 478014-27-6P 478014-28-7P 478014-29-8P
478014-30-1P 478014-31-2P 478014-32-3P 478014-42-5P
478014-43-6P 478014-44-7P 478014-45-8P 478014-55-0P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 55-22-1, Isonicotinic acid, reactions 59-67-6, Nicotinic acid, reactions 88-65-3, 2-Bromobenzoic acid 100-07-2, 4-Methoxybenzoyl chloride 102-52-3, Malonaldehyde bisdimethylacetal 107-13-1, Acrylonitrile, reactions 107-91-5, 2-Cyanoacetamide 124-68-5, 2-Amino-2-methyl-1-propanol 394-41-2, 3-Fluoro-4-nitrophenol 609-67-6, o-Iodobenzoyl chloride 619-64-7, 4-Ethylbenzoic acid 1137-41-3, 4-Aminobenzophenone 3612-20-2, 1-Benzyl-4-piperidone 4746-97-8, 1,4-Cyclohexanedione monoethylene ketal 6144-78-1, N-Methyl-2-pyridinecarboxamide 7752-82-1, 2-Amino-5-bromopyrimidine 10365-98-7, 3-Methoxyphenylboronic acid 13535-13-2, 2-Amino-5-phenylpyrazine 59489-71-3, 2-Amino-5-bromopyrazine 71597-85-8, 4-Hydroxyphenylboronic acid 79099-07-3, N-tert-Butoxycarbonyl-4-piperidone 87199-15-3, 3-Hydroxymethylphenylboronic acid 172733-79-8
173944-49-5 173944-52-0 190060-72-1 328232-95-7
328233-38-1 328233-39-2 328233-40-5 328233-41-6
328233-44-9 328233-45-0 478014-40-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 20577-26-8P, 2-Bromo-3-cyanopyridine 20577-27-9P, 3-Cyano-2-hydroxypyridine 53416-46-9P 79568-32-4P

204770-67-2P, 2-Amino-5-(4-hydroxyphenyl)pyrazine
221040-07-9P 268538-11-0P 268538-54-1P 328233-01-8P
328233-02-9P 328233-03-0P 328233-04-1P 328233-05-2P,
Spiro [cyclohexane-1,1'(3'H)-isobenzofuran]-3',4-dione
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328233-14-3P 328233-15-4P 328233-16-5P 328233-17-6P
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328233-22-3P 328233-23-4P 328233-24-5P 328233-25-6P
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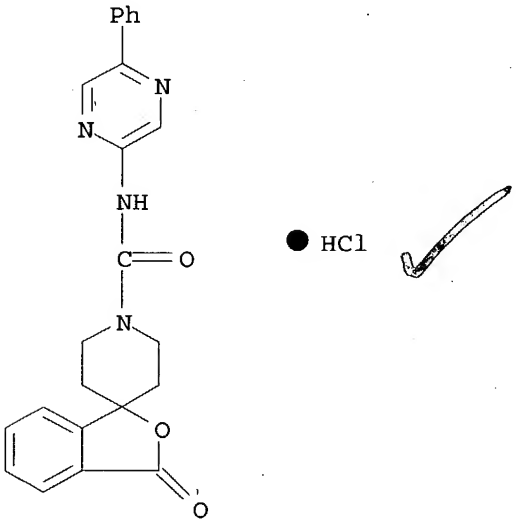
478014-39-0P 478014-41-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
IT **471257-55-3P**, 3-Oxo-N-(5-phenylpyrazinyl)spiro(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)
RN 471257-55-3 CAPLUS
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 3-oxo-N-(5-phenylpyrazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



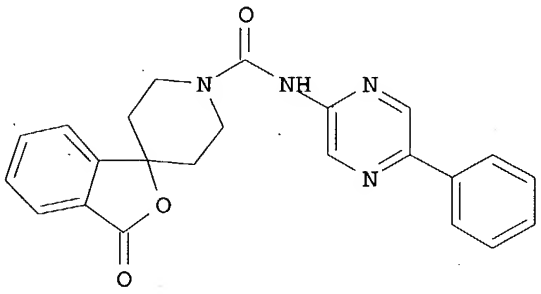
Applicant

ACCESSION NUMBER: 2002:794288 CAPLUS
DOCUMENT NUMBER: 137:310936
TITLE: Process for making pyrazinyl spiroisobenzofuranones
INVENTOR(S): Song, Zhiquo Jake; Zhao, Matthew Mangzhu
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K007-46

US PATENT CLASSIF.: 512010000
CLASSIFICATION: 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002151456	A1	20021017	US 2002-54413	20020122

PRIORITY APPLN. INFO.: US 2001-263463P P 20010123
OTHER SOURCE(S): CASREACT 137:310936
GRAPHIC IMAGE:



I

ABSTRACT:
This invention relates to a process for making spiroisobenzofuranones, in particular 3-oxo-N-(5-phenylpyrazinyl)spiro(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide (I), by coupling of an aminopyrazine fragment with a spirolactone piece. For the aminopyrazine fragment, the process in this invention involves a selective monobromination, a catalyzed Suzuki coupling, and carbamate formation steps. The synthesis of the spirolactone piece involves lithiation/addn. to 1-benzyl-4-piperidone, acid catalyzed cyclization, and deprotection by hydrogenolysis. Prior to the present invention, the monobromination of 2-aminopyrazine would produce a low yield of the desired product due to side reactions. However, the use of a flow-cell type reactor in the present invention significantly improves the yield. During the Suzuki coupling, the addn. of a stable cryst. solid catalyst with reliable quality improves the coupling. In addn., the present invention provides an environmentally sound process that eliminates the need to use pyridine as the solvent during the carbamate formation and chloroform in the final coupling. As a result, the present invention provides an environmentally sound procedure for making functionalized pyrazine compd. in good yields. For example, N-(5-phenyl-2-pyrazinyl)carbamate was prepd. in three steps: (1) bromination of 2-aminopyrazine using 1,3-dibromo-5,5-dimethylhydantoin in a flow-cell reactor, (2) coupling of 2-amino-5-bromopyrazine with PhB(OH)2 in the presence of PdCl2.bul.dppf and K2CO3, and (3) treatment of 2-amino-5-phenylpyrazine with PhOCOCl and pyridine in MeCN and THF. Lithiation of 2-bromobenzoic acid using BuLi, followed by addn. of 1-benzyl-4-piperidone and conc. HCl in THF gave 1'-benzylspiro[isobenzofuran-1(3H),4'-piperidine]-3-one.bul.HCl. Debenzylation using 10% Pd/C and coupling with N-(5-phenyl-2-pyrazinyl)carbamate in th e presence of i-Pr2NEt in DMF afforded I.

SUPPL. TERM: pyrazinyl spiro isobenzofuranone piperidine prepn aminopyrazine spirolactam coupling; spiro isobenzofuranone piperidine pyrazinyl prepn green chem

INDEX TERM:
Cyclocondensation reaction
Cyclocondensation reaction catalysts
Green chemistry
Suzuki coupling reaction
Suzuki coupling reaction catalysts
(environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines

with spirolactones)

INDEX TERM: Reactors
(flow; environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines with spirolactones)

INDEX TERM: Spiro compounds
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lactams; environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines with spirolactones)

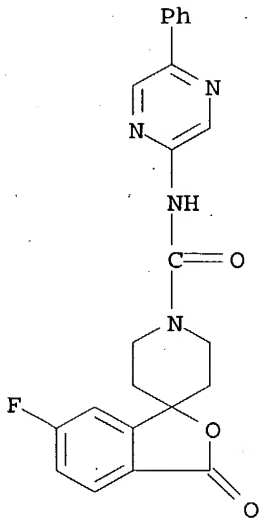
INDEX TERM: Lactams
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(spiro; environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines with spirolactones)

INDEX TERM: **471257-55-3P**, 3-Oxo-N-(5-phenylpyrazinyl)spiro(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide
ROLE: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)

INDEX TERM: 98-80-6, Phenylboronic acid 1885-14-9, Phenyl chloroformate 3612-20-2, 1-Benzyl-4-piperidone 5049-61-6, 2-Aminopyrazine 25638-04-4, Bromobenzoic acid
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)

INDEX TERM: 13535-13-2P, 2-Amino-5-phenylpyrazine 54596-01-9P, 1'-Benzylspiro(isobenzofuran-1(3H),4'-piperidin)-3-one Hydrochloride 59489-71-3P, 2-Amino-5-bromopyrazine 172733-79-8P, Spiro(isobenzofuran-1(3H),4'-piperidin)-3-one Hydrochloride 268538-11-0P, Phenyl N-(5-phenyl-2-pyrazinyl)carbamate
ROLE: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
IT **328232-34-4P 328232-36-6P 328232-57-1P**
328232-58-2P 328232-61-7P 328232-62-8P
328233-00-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)
RN 328232-34-4 CAPLUS
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 6-fluoro-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 328232-36-6 CAPLUS
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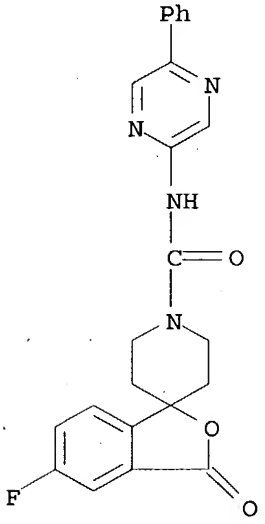

RN 328232-57-1 CAPLUS
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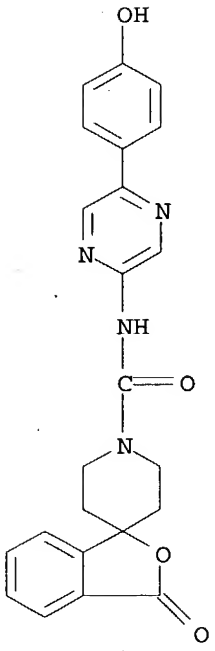

RN 328232-58-2 CAPLUS
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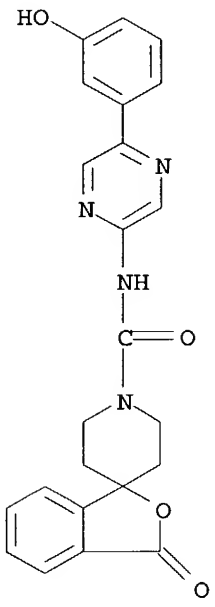
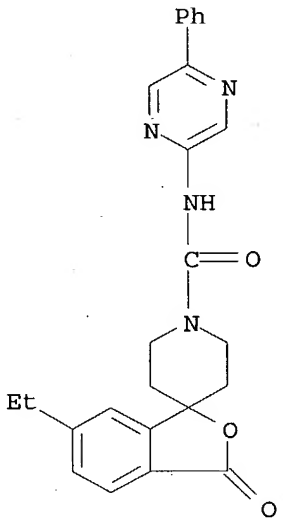


RN 328232-61-7 CAPLUS
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 6-ethyl-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 328232-62-8 CAPLUS
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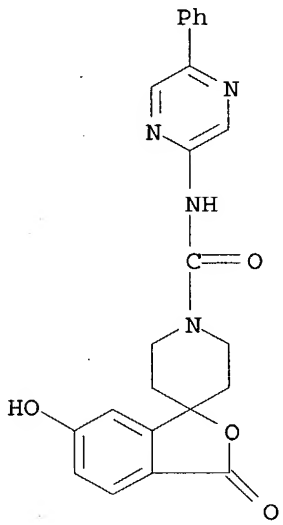
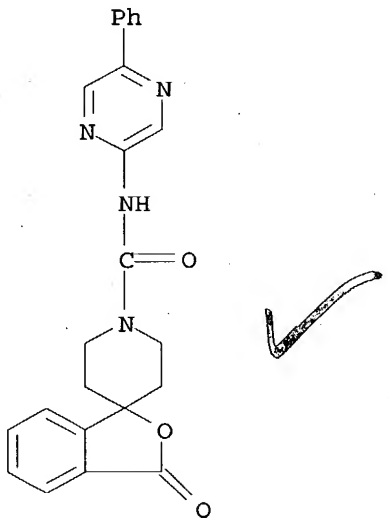


RN 328233-00-7 CAPLUS
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, 3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2001:152682 CAPLUS
DOCUMENT NUMBER: 134:207809
TITLE: Preparation of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compounds as neuropeptide Y antagonists.
INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D471-10
SECONDARY: A61K031-438; A61P009-00; A61P025-00; C07D491-10; C07D519-00; C07D307-94; C07D405-12; C07D471-10; C07D221-00; C07D209-00; C07D471-10; C07D221-00; C07D221-00; C07D491-10; C07D307-00; C07D221-00
CLASSIFICATION: 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014376	A1	20010301	WO 2000-JP5427	20000811
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013423	A	20020507	BR 2000-13423	20000811
EP 1204663	A1	20020515	EP 2000-951971	20000811
EP 1204663	B1	20031029		
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EE 200200082	A	20030616	EE 2002-82	20000811

NZ 517057	A	20030829	NZ 2000-517057	20000811
JP 2002030086	A2	20020129	JP 2000-247145	20000817
JP 3411262	B2	20030526		
JP 2003104884	A2	20030409	JP 2002-271261	20000817
BG 106390	A	20021229	BG 2002-106390	20020206
NO 2002000814	A	20020415	NO 2002-814	20020219
US 2003055251	A1	20030320	US 2002-226225	20020823
US 6649624	B2	20031118		
US 2003220499	A1	20031127	US 2003-453737	20030604

PRIORITY APPLN. INFO.:

JP 1999-233573	A	19990820
JP 2000-137692	A	20000510
WO 2000-JP5427	W	20000811
JP 2000-247145	A3	20000817
US 2000-640784	A3	20000818
US 2001-983598	A3	20011025
US 2002-101221	A3	20020320
US 2002-226225	A3	20020823

OTHER SOURCE(S): MARPAT 134:207809

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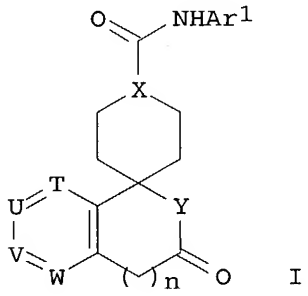

I

ABSTRACT:
Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = N, CH; Y = (substituted) imino], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide, (II), which inhibited [125I]peptide YY binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

SUPPL. TERM: spiroisoindolinepiperidine spiroisoquinolinepiperidine spiroisobenzofuranpiperidine prepn neuropeptide Y receptor antagonist; antidiabetic spiroisoindolinepiperidine spiroisoquinolinepiperidine spiroisobenzofuranpiperidine prepn; antiobesity agent spiroisoindolinepiperidine spiroisoquinolinepiperidine spiroisobenzofuranpiperidine prepn; bulimia treatment spiroisoindolinepiperidine spiroisoquinolinepiperidine spiroisobenzofuranpiperidine prepn

INDEX TERM: Neuropeptide Y receptors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(antagonists; prepn. of spiroisoindolinepiperidines,

spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

INDEX TERM: Appetite
(bulimia, treatment; prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

INDEX TERM: Antidiabetic agents
Antiobesity agents
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

INDEX TERM: Spiro compounds
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 328231-96-5P 328231-97-6P 328231-98-7P 328231-99-8P
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328232-99-1P **328233-00-7P**
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

INDEX TERM: 55-22-1, Isonicotinic acid, reactions 59-67-6, Nicotinic acid, reactions 88-65-3, 2-Bromobenzoic acid 100-07-2, 4-Methoxybenzoyl chloride 102-52-3 107-91-5, Cyanoacetamide 124-68-5, 2-Amino-2-methyl-1-propanol 609-67-6, o-Iodobenzoyl chloride 619-64-7, 4-Ethylbenzoic

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ROLE: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

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ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Banyu Pharma Co Ltd; WO 0027845 A 2000 CAPLUS
(2) Hoffmann La Roche; WO 9929696 A 1999 CAPLUS
(3) Merck & Co Inc; EP 0615977 A 1994 CAPLUS

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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